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POTENTIAL FOR TELEMETRY IN THE RECORDING OF BRAIN WAVES FROM ANIMALS AND MEN EXPOSED TO THE STRESSES OF SPACE FLIGHT

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Dr. Adey was born in Adelaide, Australia in 1922. He was educated at the University of Adelaide and graduated in Medicine in 1943. He served with the Royal Australian Navy, did post-doctoral research at the University of Oxford, England, and has been a member of the faculty at the University of Adelaide and the University of Melbourne. At present he is Professor of Anatomy and Physiology at the University of California Medical Center at Los Angeles. Dr. Adey has published more than 90 papers on brain research and is a member of several scientific societies.

I WOULD like to discuss very briefly some of the work that we have done in the past three years to test the feasibility of the telemetry of EEG's from animals and men in space flight, including the booster and re-entry phases of this type of flight. What I wish to say is in the frame of four areas: first, the development of appropriate implantation techniques to permit recording from deep brain structures; secondly, the development of special hardware for both recording of the EEG and the behavioral training; thirdly, the special testing that is involved in the environmental aspect of centrifuging and shaking during the recording, and fourthly, data analysis as a requirement in flight to minimize telemetry requirements.

This work has been conducted in the Space Biology Laboratory of the Brain Research Institute of the University of California at Los Angeles. It has enjoyed very generous support from the Air Force, both initially, and on a continuing basis, and more recently, from NASA. My chief collaborators in these studies are Wallace D. Winters and Raymond T. Kado.

In connection with the implantation, we have tested a considerable variety of techniques, comparing often in one brain different types of electrodes. Rigid electrodes consist of a staff carrying very fine wires beyond the tip of the staff. In the symmetric regions on the opposite side we have inserted very fine, unsupported wires and compared the electrical records and the histology after severe physical stresses, such as centrifuging and shaking. We have examined these brains microscopically for evidence of undue damage. As you can see, the implanted regions are very deep indeed.

The brain regions which are most sensitive to changing behavioral states and changing states of consciousness lie in the temporal lobe of the brain. We have carried out these studies in cats and monkeys and, most recently, in chimpanzees. We have also implanted other surface regions, other deep regions, but most of what I have to say concerns the responsiveness of deep brain structures in the temporal lobe.

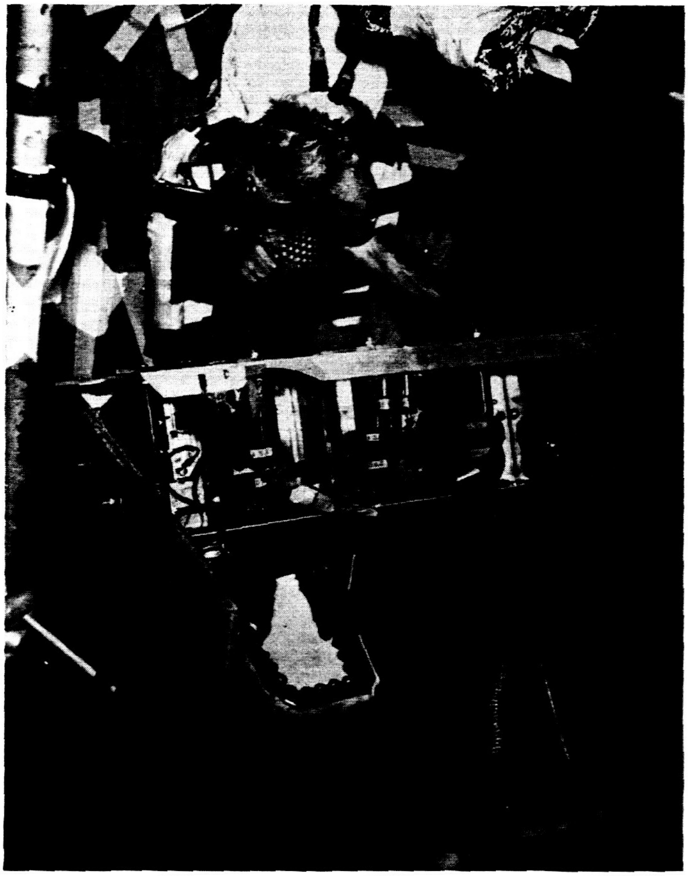


FIG. 1. A pig-tail macaque monkey with deep brain electrodes on a special chair on the arm of the human centrifuge at University of Southern California. His brain activity is recorded as he makes a discriminative choice on the behavioral test panel in front of him. The lead attachments to his head are clearly visible.

It is often asked whether it is possible to implant such electrodes in the brain without causing undue damage in the course of centrifuging and shaking. However, in studying the after-effects of repeated centrifuging to 8 or 10 *g* and repeated shaking in animals finally sacrificed some months after the last test, the degree of gliosis around the electrode tract is no more than one would expect in an uncentrifuged animal. In other words, one does not get, as I have often heard suggested, a shearing damage to the brain because it is sliding around inside the skull like a bowl of jelly. Whatever it may be, the brain certainly does not behave in that fashion, and we have checked this in many ways and on many occasions.

In Fig. 1 you see a monkey in a restraining chair on the human centrifuge. The method of connection to the amplifying system is through two small plugs carrying some eighteen connections, and the wire itself, the orange colored cable, is a special type of missile cable designed to minimize what is so devastating an effect in this type of procedure ... namely, the building up of a static charge on the cable which will totally conceal the very small potentials that one is trying to record. In this cable, there is a special aluminum powder deposited between the inner and outer aspects of the braid sheath and this cable can be deformed in a most incredible way without the appearance of any artifact.

Most recently, we have implanted in the same way the chimpanzee. This three-year-old male has been adapted in the chair to accept restraint and has the usual plug arrangement on his head. The placements were on the basis of more than one year's work in the preparation of what we call a stereotaxic atlas, that permits the approach to any part of the brain with an accuracy of about 1 mm, provided one knows the body weight and, particularly, of course, the head size. This, incidentally, is the first chimpanzee ever to be implanted in this way and, in fact, the first chimpanzee, as far as I know, from which any brain wave recording has been done.

EQUIPMENT TECHNIQUES

In terms of the special hardware, some years ago we developed an amplifier which has proved a regular workhorse. It is a complete EEG channel with a gain of about 40,000, extremely rugged; all thermally sensitive components are in a block of magnesium alloy. After completion and testing, it is embedded in epoxy resin. It has been shaken at 25 *g* peak to peak while operating at full gain, with the shaking at five to two thousand cycles per second. It has a minor resonance at 750 cycles, but this does not in any way interfere with its performance characteristics. It is extremely rugged and capable of withstanding almost any conceivable force that can be imposed upon it. One can actually use it as a hammer while operating.

The next development is a relatively recent one, in which, primarily for purposes of manned space flight we have developed a microminiaturized amplifier which is incorporated in an electrode for attachment to the scalp (Figs. 2 and 3). It consists of a three-stage transistor amplifier mounted

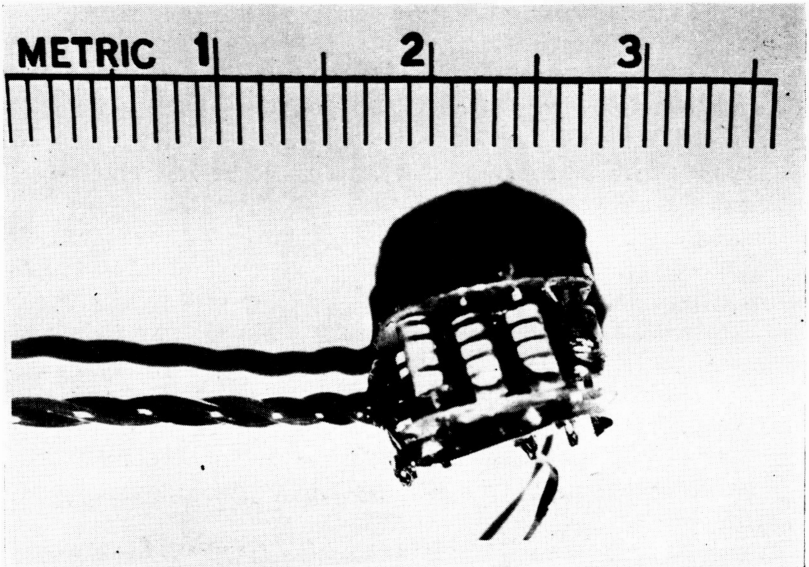


FIG. 2. A microminiaturized three stage transistorized preamplifier less than a half inch in diameter and less than a half inch high, developed for picking up the EEG from the scalp in man and animals. All connections are made with welding techniques.

FIG. 3. A completed amplifier-pickup electrode containing the amplifier shown in FIG. 2, and enclosed in a stainless steel case. The gasket at the lower rim provides a firm scalp attachment.

between two nylon wafers. The whole device is less than a half-inch in diameter and less than a half-inch high. It is embedded either in epoxy or silastic plastic and attached to its base is the pick-up electrode from which the scalp EEG will be obtained. Finally, it is placed within a stainless steel top hat

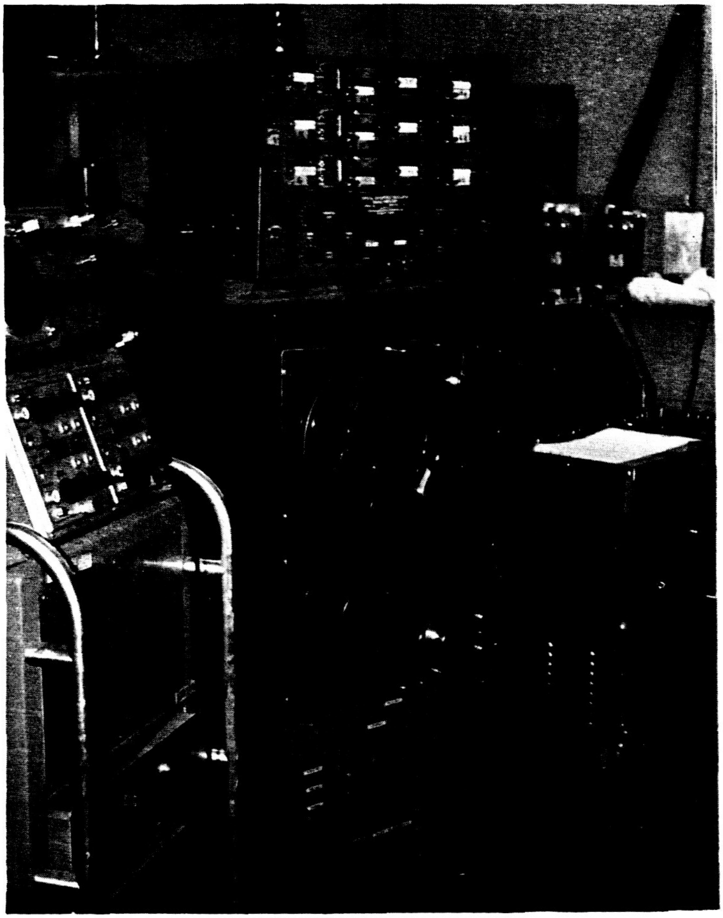


FIG. 4. The F.M. multiplex system of tape recording developed for recording of brain wave data. The subcarrier oscillators and mixing system are mounted on top of the tape transport. The system permits recording of as many as 14 channels of information on one tape track. It is extremely rugged and ideal for field use.

which provides a great degree of shielding. The actual pick-up is from the lower surface through a sponge which is soaked in electrode paste. The attachment to the scalp is through a cork gasket. For those who are electronically minded, the input impedance of this device is around 150K, so that a pair of them in a differential arrangement have an input impedance of

300,000 Ω, and the output impedance is only 1500 Ω, so that it is inherently very resistant to any artifacts arising from the shaking of the cables as the person or the animal turns his head. The gain is about 100 so that the EEG comes up to the millivolt level, which can be applied directly to low level telemetry subcarrier oscillators.

In the centrifuge experiments, we have developed a behavioral test panel which is similar to the initial design adopted at Holloman Air Force Base to test the chimpanzee's discrimination. Three boxes project symbols, three at a time, on little screens in front. The animal recognizes the odd one of the three, presses it, and receives a food pellet in reward. The difference from the Holloman programmer is that the sequencing here allows several million programmer combinations before it comes back to the same one. As you may have noticed with the chimpanzee or intelligent monkey, if there are only a few sequences by reason of the limited number of symbols, they learn the sequence very quickly and pay very little attention as they press the bar.

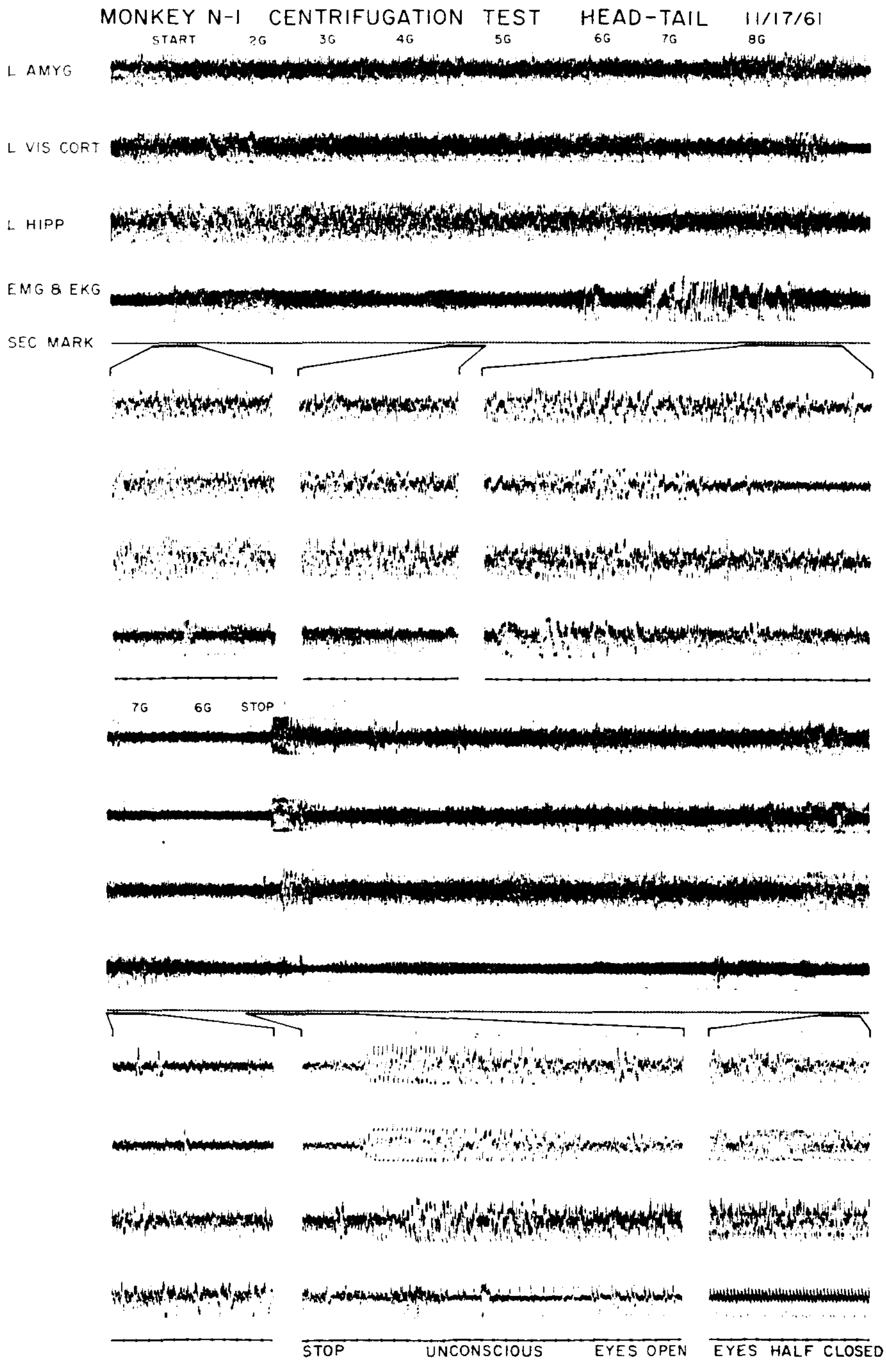
The approach in our laboratory to problems of telemetry has been through the use of standard IRIG subcarrier oscillators. There has been a dividend as far as our laboratory work is concerned, in that by the use of this technique, with a standard twin-track recorder, one can have as many as 28 channels of data placed on the two tracks, with 14 channels per track. Within certain constraints on band-pass and required limitations on signal amplitude, it is an exceedingly flexible system with worthwhile dividends in certain computations where arrangement of multichannel stacked heads can lead to problems between different recorders (Fig. 4).

TESTING TECHNIQUES

To turn to the special testing, we have had the enthusiastic co-operation of the University of Southern California in the use of their human centrifuge. It is a large device reaching accelerations up to 10 g for man or animals.

We have tested monkeys in a discriminative situation during centrifuging through the full Atlas booster profile, confined them in a simulated capsule in 14-day simulated orbital flights, in which they feed themselves on the basis of

Fig. 5. Sample records of brain waves (top 3 leads in each panel), and electromyogram and electrocardiogram (lead 4) during centrifuging to a blackout. The first and third panels of the record show at slow speed the continuous record as the blackout develops, and subsequent recovery. The second and fourth panels show expanded portions of the record, and reveal details of brain activity. Blackout begins at the right end of the top panel, as the acceleration reaches $8g$. The EEG flattens severely during the blackout. As the centrifuge stops (panel 3) recovery of the EEG pattern is through a series of electrical seizure discharges. Details of these seizure discharges can be seen in the middle portion of the lowest panel. Abbreviations: L. AMYG., left amygdaloid lead (deep temporal lobe of brain); L. VIS. CORT., left visual cortex; L. HIPP., left hippocampus (deep temporal lobe of brain); EMG & EKG, electromyogram and electrocardiogram. From Winters, Kado and Adey, 1962. **(Figure opposite)**


MONKEY N-1 CENTRIFUGATION TEST HEAD-TAIL 11/17/61
START
2G
3G
4G
5G
6G
7G
8G
L AMYG
L VIS CORT
L HIPP
EMG & EKG
SEC MARK
7G
6G
STOP
STOP
UNCONSCIOUS
EYES OPEN
EYES HALF CLOSED

their discriminative performance, and then come through a much more severe acceleration resembling the re-entry profile.

In the cat, for instance, during increasing transverse acceleration to 8 g, here is in the deep temporal lobe structures a tremendous increase in the amount of regular rhythmic wave discharge. As the acceleration is sustained at that figure, that type of activity dies away. It is not until one commences the deceleration that it builds up again and dies away as the centrifuge becomes stationary. If one changes to a longitudinal acceleration, producing a blackout, in the induction of the blackout there is a very unusual spike-like type of electrical discharge which is actually epileptic in form. It arises in the deep leads of the temporal lobe; it can spread and become general with muscular movement and other aspects of a typical motor seizure or, it may remain without any motor concomitants, although the judgment and discrimination, of course, are lost or grossly impaired at this time.

In the monkey, one finds similar effects in longitudinal acceleration with blackout. The animal goes unconscious with flattening of the record and if the acceleration is rapidly reduced, return of consciousness is through a period of these seizure discharges. (Fig. 5.)

We began two years ago to examine the effects of shaking, with the monkey enclosed in a partial pressure suit of foam plastic. More recently we have used a different technique, with the animal on a chair resembling a satellite couch. We have been generously assisted by the Douglas Aircraft Company in these studies. Our interest in vibrations as a physical stress is enhanced by the findings — as yet unconfirmed — that Titov may have suffered cerebral damage on account of the shaking of the big booster that he rode. This I mention merely in passing because it is a hearsay report at this time.

Briefly, there is a driving of the brain wave rhythms at the rate of the shaker particularly around 10 c/sec. When we saw this first we suspected that it was nothing more than an electromechanical artifact, although there were resonance bands where it appeared and other frequencies where it would disappear; it would appear differentially in different brain regions at different times, and so on. More recently we have found that it disappears if one anesthetizes or kills the animal. Thus, it is not an artifact and it is something which indicates a gross abnormality of the rhythms induced by the shaking. We have not seen prolonged after effects. In fact, animals shaken two years ago are in very good condition (Fig. 6). So I don't know whether one can anticipate any permanent change.

We have considered the question of the usefulness of the EEG record in prolonged space flight, where an assessment will be necessary of sleep-wakefulness cycles, for example. We have recorded both from the surface and deep structures of the chimpanzee's brain continuously from the alert state to the onset of drowsiness, with urination and drooping eyelids. The appearance of regular bursts of waves signals the onset of sleep and one does not need to be an expert in EEG to see that as the animal sleeps and wakes by turns, the recurrent bursts of high amplitude waves make what we call a "spindling" record. As he finally wakes up, sits up and looks around, there is a return to the alerted pattern (Fig. 7).

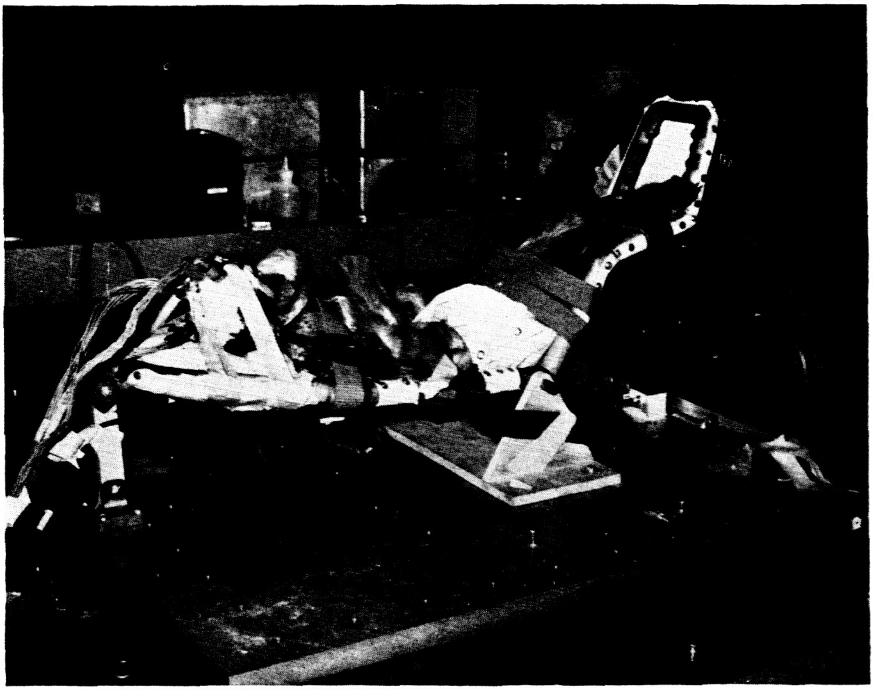


FIG. 6. Monkey on shaking table at Douglas Aircraft Company, Santa Monica. Brain electrical activity from surface and deep brain structures recorded during shaking over a spectrum from 5 to 40 c/sec has shown distortion of brain wave patterns by the shaking at certain bands of frequencies. Accelerometers on head and body indicate amount of acceleration.

Thus, this is one area where we now are sure that the EEG will give very valuable information. There is reason to think that there may be disturbance of the sleep-wakefulness cycles in prolonged weightlessness. The evidence from the dolphins suggests that they sleep very little. Man made buoyant and in an environment with which he is in equilibrium both temperature-wise and without skin cover also appears to sleep very little, and this we feel is worthy of further investigation.

METHODS OF DATA REDUCTION

Finally, we come to the question of reduction of the amount of data that should be telemetered. If we can get around this problem of sending black masses of "raw" records, it would be very advantageous both to the nature of

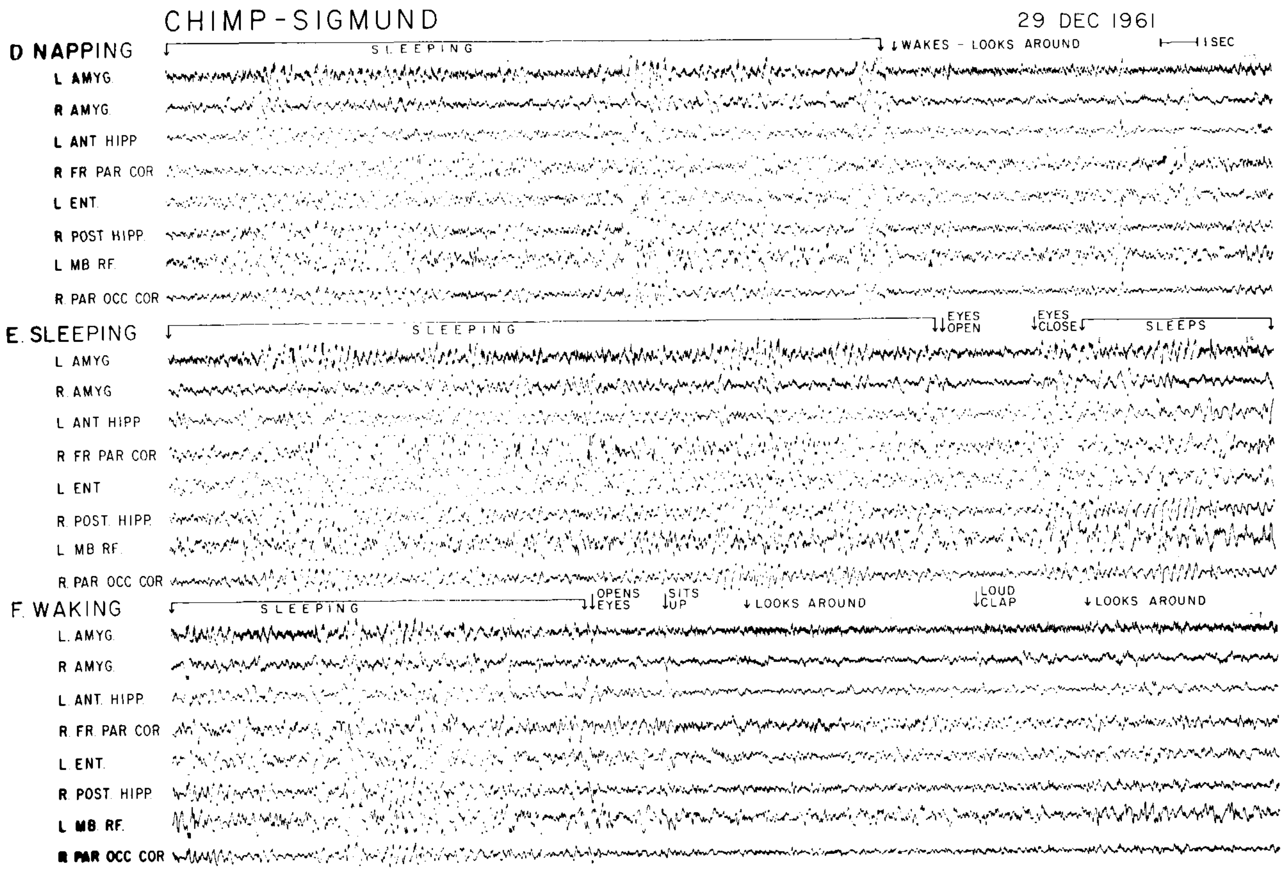


FIG. 7. Electrical brain activity from surface and deep structures of the first chimpanzee ever implanted with chronic brain recording electrodes. The records clearly show the onset of regular, rhythmic high amplitude wave trains as attention waves and brief "napping" occurs and sleep begins. These records in fatigue and sleep are clearly different from the faster, lower amplitude, less regular patterns in the alerted animal. Lead abbreviations: L. AMYG and R. AMYG, left and right amygdala (deep temporal lobe regions of brain); L. ENT, left entorhinal cortex (deep temporal region); L. MB. RF., left midbrain reticular formation (lower brain stem core); R. FR. PAR. CoR. and R. PAR. OCC. CoR., surface leads from frontoparietal and parietooccipital cortex.

the experiment and probably to the validity of the read-out. In one of my laboratories we are engaged in studies of the most appropriate forms of tape recording and data reduction, and the output from this laboratory can be fed into the large IBM 7090 computer in our campus computing facility. We will have a similar instrument in the Medical Center for our own use shortly. I merely propose to outline the sorts of things that one can do, because they exemplify the value of the interface between the engineer and the biologist. I am an incurable "do-it-yourselfer," but, nevertheless, I think that the types of information that we have been able to retrieve from brain wave records during a discriminative task exemplify very clearly the value of our association with engineers.

In the typical record from an animal preceeding and during the period of discriminative approach to food, the so-called "pre-approach" epoch and the "approach" epoch are very different in the nature of their wave patterns. Our records are frequently all from deep leads except one, which comes from visual cortex, and we would like to analyze, as simply as possible, the nature of these wave processes. This can be done in its simplest form by the "autocorrelation" type of technique. It shows significant differences between "pre-approach" and "approach" records, and we have been surprised to find that we can tell the difference between correct and incorrect performances on the basis of these computer analyses.

For example, one can by "cross-correlation" analyze phase patterns between different brain regions. In correct responses, there are certain phase patterns—I will not detail here how we measure the phase—and in the wrong responses, these are different. We have compared the data from different training days and have found that the right responses have similar phase patterns on different days, and that wrong responses likewise have certain identical phase patterns on different days, and that the latter patterns differ from those in correct responses. This is a very interesting application of a technique well known to the mathematician and engineer for analysis of such problems as missile vibration, and which is now achieving some place in the analysis of brain data.

We have used much more complex forms of analysis which allow us to look at the interrelations of phase and amplitude across a spectrum of frequencies. This type of "cross spectral" analysis was also designed initially for analysis of missile vibration data. With it, we can examine, for example, phase relations between two brain regions across a spectrum from 2 to 20 c/sec. As an example, the phase pattern in a correct response was found to be consistently at plus 30 degrees from 2 to 12 c/sec. By contrast, the next approach that the animal made to the food was an incorrect one, and a big change appeared with a reversal from plus 90 degrees to minus 90 degrees at about 5 c/sec in the phase angle. We have observed such differences in different animals, in different situations and the consistency of the difference in phase patterns between correct and incorrect responses is very striking.

We have also used a mathematical technique which, again, was developed to examine the magnetometer records from a spinning satellite. In this situation, variations in the earth's magnetic field produce a very small phase modulation on an apparently sinusoidal output. If the earth's magnetic field was constant, there would be no phase modulation; the output would be a perfect sinusoid.

We have applied this analytic technique to the trains of waves appearing during discriminative approach to food, where the wave trains appear to have almost a single frequency. The results indicate that there is a modulation of what is essentially the "center frequency" of the activity around 5.5 c/sec. This modulation appears only at moments of maximal attention.

I am aware that it is not the purpose of this meeting to discuss in detail the question of interpretation of data. I will therefore merely emphasize that through this type of study one can make very meaningful examinations of quite complex records and that the form of computation is compatible with its telemetry from a space environment.

DISCUSSION

DIETZ: Dr. Adey, in the correlation techniques which you are using, have you considered the possibility of collecting the data initially in a digital form, and then processing it from there?

ADEY: Yes, as a matter of fact, by the beginning of next month, we will have an analog-to-digital conversion system which will take on-line data and feed it on-line to a medium-sized instrument computer. This will be an Airborne Instruments system of A-D conversion with a maximum conversion rate of 200 K per second and a Control Data corporation 160-A form of spectral analysis. In about six months we hope to utilize the facilities of the new Medical Center Computing facility, as well as our own smaller instalation, in the hope that at least some of the more complex analyses may be available on-line.

DIETZ: Is this going to be quantitative analysis of the over-all environment, or are you going to reduce the data to the effects on any one of the senses of the animal, like his sense of hearing, or any one of the others, so that you can run some correlation of the environment to the effect of any one of the senses that he has?

ADEY: I would imagine that it would be total examination of the environment as well as the animal's performance, but bear in mind that we are going to have repeatedly programmed into the animal's behavior time-locked events. These will provide the zero time from which most of these correlations will be achieved.

MCCULLOCH: I don't own any stock in any computer corporation, but I should tell you that TXO has a successor known as PDP-1. It's about three feet wide and about five feet high and about six or seven feet long, and you plug it into the house current. Normally, it takes a biologist one night to learn the programming. This, I think, is one of the places where the engineer and the biologists are getting together.

SCHMITT: Well, since you mention this, you must also mention that its little brother is being developed specifically for biologists, and it's going to be easier to program and much less expensive.

MULLINS: And I noticed at the IRE show that somebody has come out with an auto-correlator which is just like a set of Ampex tape recorders.

CLYNES: In connection with the correlator, we've had a correlator similar to what Dr. Adey has mentioned in our lab since August or September. It does on-line cross-correlation in digital form. I don't have any records with me, but you're welcome to drive to Rockland

State Hospital to see this thing in operation. We've correlated brain activity from various parts on-line as well as seismic events, and it's certainly a valuable tool.

DIETZ: Dr. Adey, in talking about computers, we don't make computers nor do I own any stock in computers. But recently Dr. Tunturi of the University of Oregon, who did a study to try to determine what type of computer he should use in some experiments he's doing very similar to Dr. Adey on correlation techniques, came up with the fact that there are about five or six appropriate computers. I'll just briefly mention them: CDC 160-A, the PDP-1, the GE-225, and IBM 1410, and the IBM 1620, and the National Cash Register 315 and the Packard Bell 250. Of these, most range in about the $200,000 category, but IBM offered a 60 per cent discount as the selling feature and they got the contract. So on medical research, IBM offered a pretty good set of three programs and a 60 per cent discount, and it was hard to beat it even though some of the other computers might have been better.

ADEY: I don't have any stock in any computer companies either—but the IBM 1620 is slow and it is almost impossible to do any of the on-line experiments of which you speak, with this particular instrument.

IRVINE: We might add one thing there, Ross, that both the CDC and PDP-1 have as virtues very flexible input output equipment, display copes, and so on. The 1620 simply is not this flexible.

CORSON: I wonder if I may return to the colloquy of living things. Did shaking equally modify brain waves from all regions of the body or was it selective in any particular ones; and, secondly, could you study their nature by, say, modifying them by certain classes of tranquilizing agents, say, phenothiazines or muscle relaxants to see where the origin of damage lies?

ADEY: Our particular interest, in fact, lies in the sources of the tremendous barrage of impulses which are apparently capable of modifying the brain wave pattern. The problem narrows itself essentially to two fields. One is the input from muscles and joints; the other one is from the vestibular apparatus in the ear.

In terms of the brain regions which show the most responsiveness, there are in the brain stem reticular substance or so-called "core" of the brain, some primary sensory control areas, and the temporal lobe region. These are also the regions in which in the rhythm patterns are most apparent during a discriminative performance for food. The visual cortex is activated even if the animal is blindfolded. We have conducted some experiments with the monkeys blindfolded because we wanted to eliminate the factor of visual stimulation. There thus appear to be certain defined brain systems which show a preferential susceptibility. We do not yet know anything about the ways in which this activation occurs.

DELGADO: In this differential study you did, it was not clear which were better: the rigid or the flexible electrodes? My second question is: In the recovery after the acceleration, which area of the brain showed the higher sensitivity? By temporal lobe, I think that perhaps you mean hippocampus mainly and not the cortex or some other area of the brain.

ADEY: Very interestingly, the hippocampus does show a slow recovery following longitudinal centrifuging. It takes as much as 30 seconds to one minute to recover but the amygdala is even slower. Its electrical patterns may remain disordered for two or three minutes.

Secondly, in terms of the evaluation of the electrodes, we adopted the following procedure. We implanted and trained the animals, so that we had very considerable amounts of EEG training records. After centrifuging we examined the records very carefully for alterations in rhythm patterns and sought alterations in the animal's behavorial performance. The results indicated no difference between the flexible and the rigid electrodes.

In the histological studies, the rigid electrodes did show a small amount of tearing up near their point of entry into the brain. In the deeper parts of the brain, below, say 10 or 15 mm, there was again very little difference between the findings in centrifuged and uncentrifuged brains. It appears that in the sort of acceleration that we have used, the brain is probably behaving like a viscous liquid with a streamlined flow, so that there is a shearing between layers, but because of viscosity it is only the layers of brain which are closest to the surface that are maximally affected this way. I don't know, but this is the way it seems to us.

MACKAY: Was the electrode direction usually normal to the acceleration?

ADEY: No, they were all over the place.

McCulloch: In getting out your curves on phase shifts, what was the method of your calculation?

Adey: Well, the present approach was with cross-correlation analysis. The first data was key punched from paper written records. More recently we have done the same thing with magnetic tape records. The latest analysis are based on a very comprehensive computer program that was written by Tukey for Convair, as a missile vibration program, which gives auto-correlations, cross-correlations, auto-spectra, cross-spectra and coherence.

As a matter of interest—this is perhaps defeating my case—if one takes 200 sec of real time data of four EEG channels and samples each channel 167 times a second, which, after all, is not a great deal of data, it takes an IBM 7090 computer, efficiently programmed, 90 min to examine that data. So it isn't exactly data compression.